

Cancel claim 2 and rewrite as new claim 7.

--7. A corticoid 17,21-dicarboxylic ester or corticosteroid 17-carboxylic ester 21-carbonic ester of the formula I as claimed in claim 1, wherein R(1), A, Y, Z, R(3) and R(4) are defined as in claim 1, and wherein R(2) is . --

## REMARKS

#### Election/Restriction

Applicants note the Examiner's discussion of the election and restriction requirements on pages 2 and 3 of the Office action. The Examiner is correct in her assumption that the election of Group I, claims 1, 2, 4, and 5, and of the species of Example 6, of record, carry forward to this application. The Examiner is reminded that these elections were made with traverse, and the same is incorporated herein by reference.

### Duplicate Claims

Claims 1 and 2 are objected to under 35 U.S.C. § 101 as being substantial duplicates. Claim 2 has been amended to now recite only one species of the genus of claim 1. This objection has been overcome and should be withdrawn.

Claim Rejections - 35 U.S.C. § 102

Claim Rejections - 35 U.S.C. § 103

Before considering these art rejections, applicants wish to discuss the above amendments to the claims. In claim 1, R(1) is now defined as unsubstituted phenyl or phenyl substituted by one to three substituents selected from the group consisting of methoxy, chlorine, fluorine, methyl, trifluoromethyl, acetamino, acetaminomethyl, t-butoxy, t-butyl, 3,4-methylenedioxy, BOC-amino, amino and dimethylamino as disclosed at page 65, lines 11-21 of the specification. Similarly, in amended claim 1, n is zero, and (C<sub>1</sub>-C<sub>4</sub>)-alkyl is now defined only as saturated, branched by further alkyl groups with m being 1. Thus, the 21-side chain effectively becomes -O-CO-[(C<sub>1</sub>-C<sub>4</sub>)-alkyl]-phenyl, with the phenyl being unsubstituted or substituted as discussed above. These amendments have the effect that esters, i.e. 21-phenyl carboxylates, including (substituted) 21-phenyl acetates and propionates are claimed and these are neither taught nor suggested by the cited prior art.

As the Examiner is aware, and as set forth in MPEP § 2131, to anticipate a claim, the reference must teach every element of the claim.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

*Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

"The identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

As the Examiner is also aware, and as set forth in MPEP § 2143, in order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

With further regard to the first criterion, it is clear from MPEP § 2143.01 that the prior art itself must suggest the desirability of the claimed invention.

"In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary

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skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 458 F.2d 1013, 173 USPQ 560, 562 (CCPA 1972).

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

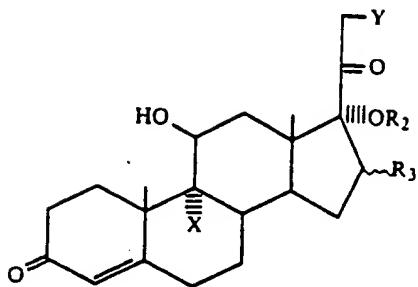
Claims 1-2 and 4-5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Villax et al. ('693) for the reasons on pages 4 and 5 of the Office action.

Claims 1-2 and 4-5 are also rejected under 35 U.S.C. § 103(a) as being unpatentable over Villax et al. ('693) for the reasons on pages 6 and 7 of the Office action. These rejections are respectfully traversed.

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Villax et al. teach compounds of the formula



wherein the Y substituent corresponds to applicants' side chain in position 21 of formula I herein, and wherein the OR<sub>2</sub> group corresponds to applicants' -CO-R(2) in position 17. Y of Villax et al. can be (*inter alia*) a benzoyl group (see col. 1, lines 64 and 65) but cannot be a group such as a C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>-CO- or C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CH<sub>2</sub>-CO- group. Therefore, no 21-phenyl carboxylates such as 21-phenyl acetates or 21-phenyl propionates are disclosed or suggested. One skilled in the art knows that a steroid molecule can be modified at numerous sites. Indeed, Villax et al. disclose a list of contemplated modifications in column 4. However, since this reference fails to teach or suggest the present invention as now claimed, these rejections have been overcome and should be withdrawn.

Claims 1-2 and 4-5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kamano et al. ('172) for the reasons on page 5 of the Office action.

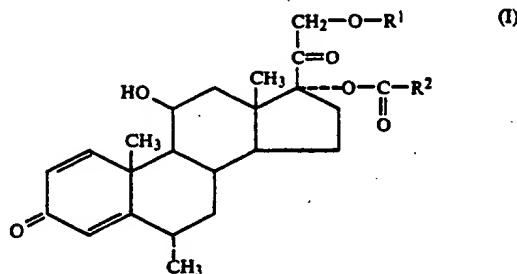
Claims 1-2 and 4-5 are also rejected under 35 U.S.C. § 103(a) as being unpatentable over Kamano et al. ('172) for the

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reasons on pages 7 and 8 of the Office action. These rejections are respectfully traversed.

Kamano et al. disclose a  $6\alpha$ -methylprednisolone of the formula I



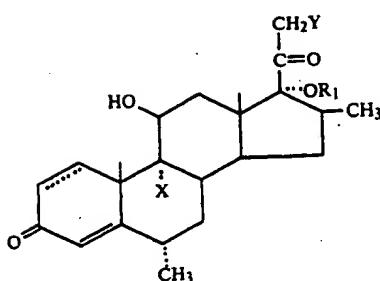
in which the  $R^1$  substituent corresponds to the portion of the side claim in position 21 of the presently claimed esters beginning with the  $C=O$  group.  $R^1$  of Kamano et al. can be  $-(CO)-R^3$  with  $R^3$  being a phenyl group (see col. 2, lines 55-61). However, there is no teaching or suggestion of the claimed 21-phenyl carboxylates such as a 21-phenyl acetate or 21-phenyl propionate. Since this reference fails to teach or suggest the present invention as now claimed, these rejections have been overcome and should be withdrawn.

Claims 1-2 and 4-5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Annen et al. ('451) for the reasons on pages 8 and 9 of the Office action. This rejection is respectfully traversed.

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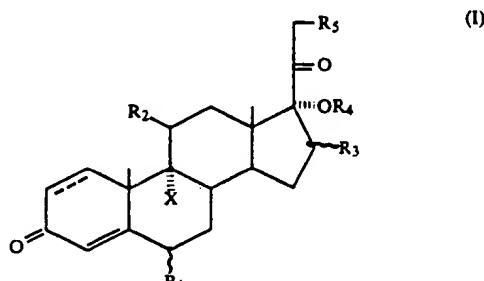
Annen et al. ('451) disclose compounds of the formula I



in which the Y substituent corresponds to the portion of the side chain in position 21 of the presently claimed esters beginning with the oxygen following the CH<sub>2</sub> group. The Y substituent of the reference can be benzyloxy (see col. 1, lines 40-41) but there is no teaching or suggestion of a 21-phenyl carboxylate such as the 21-phenyl acetate or 21-phenyl propionate now included in the claims herein. For the reasons given above, this rejection has been overcome and should be withdrawn.

Claims 1-2 and 4-5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Page et al. ('971) for the reasons on page 9 of the Office action. This rejection is respectfully traversed.

Page et al. ('971) teach a process for the preparation of esters of the formula I



in which numerous definitions for the substituents  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ , and  $X$  are disclosed. The  $R_5$  substituent of *Page et al.* corresponds to the portion of the side chain in position 21 of the presently claimed esters beginning with the oxygen following the  $CH_2$  group.  $R_5$  of *Page et al.* can be, *inter alia*, also  $R_6$ ; and  $R_6$  can be, *inter alia*,  $OR^7$  where  $R^7$  is an acyl group of the formula  $R'CO$  with  $R'$  being, *inter alia*, (ii) an aralkyl group of 7 or 8 carbon atoms (see the Abstract and col. 21, lines 1-40). Applicants have advised the undersigned that, by following this complicated procedure, it might be possible to construe a compound such as a 21-phenyl acetate or 21-phenyl propionate. However, there is no teaching or suggestion in the reference to modify the molecule in this very particular manner, especially in view of the multiple possibilities. In addition, a similar very special selection would have to be made with respect to  $R^4$  of the reference, from which the variant (iii) i.e. a phenyl group, would have to be simultaneously chosen. As set forth in MPEP § 2143.01, the fact that a reference can be modified is not sufficient to establish *prima facie* obviousness.

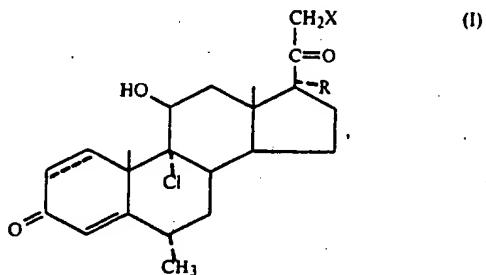
The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of

the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

This rejection has been overcome and should be withdrawn.

Claims 1-2 and 4-5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Annen et al. ('763) for the reasons on page 10 of the Office action. This rejection is respectfully traversed.

Annen et al. ('763) disclose compounds of the formula I



in which the X substituent corresponds to the portion of the side chain in position 21 of the presently claimed esters beginning with the oxygen following the CH<sub>2</sub> group. The X substituent of the reference can be benzyloxy (see col. 8, line 54) but there is no teaching or suggestion of a compound such as the 21-phenyl acetate or 21-phenyl propionate now included in the claims herein. For the reasons given above, this rejection has been overcome and should be withdrawn.

In view of the amendments to the claims and in light of the above remarks, it is urged that this application is in condition

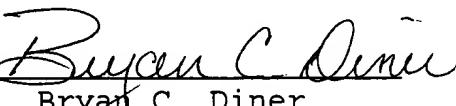
for allowance. An early and favorable action is earnestly solicited.

Respectfully submitted,

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